and truncating the analysis. **RESULTS:** The survival outcomes produced by the model are presented graphically to illustrate the impact of the different methods, along with the magnitude of change in the incremental benefits and the resulting incremental cost-effectiveness ratios (ICERs) using the various methods compared to the standard approach. Conclusion: Capturing and quantifying the structural uncertainty in partitioned survival analysis is not well developed in the literature. This study demonstrates the considerable uncertainty and the potential for bias from choosing one method of extrapolating outcomes for an economic evaluation using a partitioned survival analysis. The study also proposes options for exploring the uncertainty in order to present a balanced analysis and avoid bias in economic evaluations for oncology research.

PRM145

THE CHALLENGES OF PILOT TESTING TRANSLATED PRO MEASURES WITH CHILDREN

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INTRODUCTION: PRO measures aimed at child respondents are generally developed with the input of children from the target population, although in certain cases their age or medical condition can have implications that make this less feasible. This extends also to the translation and linguistic validation of these measures, where the usual standard of pilot testing translations with the target population may not be appropriate or beneficial. This presentation investigates the challenges of pilot testing translations with children, and explores alternative validation methods. **BACKGROUND:** Current guidelines advise that translated PRO measures should be tested with patients from the target population to best assess the measures' suitability. From our own findings, pilot testing with children can be very successful as they give more creative answers during cognitive interviews, and they can be more willing to give open, honest answers than adults. However, the success of pilot testing with children can vary depending on their age. Younger children may have too limited a vocabulary to express concepts in their own words, or may struggle to understand the cognitive debriefing process. Additionally, in some circumstances there may be ethical issues involved when asking ill children to decide whether to participate in this process which may be difficult for them to understand. **ALTERNATIVES:** Alternative methods must aim to establish the same information that would be obtained from the target population: i.e., whether the translation is appropriate for that group. Therefore we propose review processes involving parents, teachers, paediatric nurses or clinicians, depending on the measure's content and target age range. **CONCLUSION:** In some cases it is possible to successfully pilot test translated PRO measures with children, and it can be the optimum solution, where practical. However, reviews by parents or suitably qualified professionals are useful alternatives where testing with children might not be feasible.

PRM146

QUANTIFYING THE IMPACT OF PROGRESSION ON SURVIVAL IN ONCOLOGY: AN APPLICATION OF STATISTICAL MODELING FRAMEWORK TO MEASURE THE IMPACT OF EVENTS ON SUBSEQUENT RISKS

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In many diseases, the occurrence of a clinical event (e.g., stroke) can change the risk of other, usually more serious, events (e.g., death). Quantifying the impact of the first event and factoring this into assessment or extrapolation of the risk of the second event is important for clinical understanding of the disease as well as health economic assessments of new treatments. For instance, in oncology, understanding the impact of progression of disease on the risk of dying can be vital for projection of overall survival, which is often only partially observed in trials. Proper understanding of the impact of the event requires consideration of not only the occurrence of the event, but also its timing and the possibility that its effect changes with time following the event. For instance, patients who progress early after initiation of treatment may be subject to a greater increase in risk of death than a patient who progresses, say, a year after treatment. Similarly, once progressed, the increase in mortality may be highest soon after the event and gradually decline among surviving patients. We will outline a statistical modeling framework designed to quantify these various dimensions of the impact of events using Cox regression models with time-dependent covariates and effects (i.e., coefficients) to reflect the timing of event (TE) as well as time elapsed since the event (TSE). The model produces estimates that have direct clinical relevance; for instance, the coefficient for TE provides an assessment of the benefit of delaying progression, while TSE reflects whether and for how long the increase in mortality is sustained and whether it ever returns to the level of patients who had not progressed. The parameterization of the model will be illustrated with example code and analyses of example data.

PRM147

AUTOMATIC CREATION OF DISEASE MODELS USING DATA MINING TECHNIQUES ON DATA FROM A CLINICAL CANCER REGISTRY

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OBJECTIVES: Health economic disease models are often build with data from clinical trials and thus do not necessarily reflect the routine care situation in hospitals. For this scenario, we outline a method to generate disease models using data mining algorithms on patient records from a regional clinical cancer registry. **METHODS:** Markov models are a common technique in decision making. Their structure of states and transitions reflects the progress of a disease. We define a disease state as a set of features which represents a specific state of illness, e.g., diagnosis of breast cancer in HER-2-positive (human epidermal growth factor receptor 2) women who are treated with chemotherapy and mastectomy. In particular, a feature can consist of several attributes, e.g., HER-2 status can be described with the attributes 0, 1+, 2+, 3+. States: A feature selection is executed by a modeler who decides which set of features describes a disease state or patient cohort best. For identifying the most relevant attribute combinations a cluster analysis is applied beforehand. Transitions: Patients remain in one particular state as long as they match the predetermined features and attributes. Otherwise, a change to another state occurs. Thereby, a sequence of states for each patient is defined. As a final step, these sequences are used for deriving a model structure. **EXPECTED RESULTS:** Markov models backed up by real-life patient records. As a result of the automatic generation process models can be used for validating hypotheses or comparing outcomes for different patient cohorts. Therefore, the usage of such models is not strictly limited to health economic analysis. A first validation indicates the feasibility of the outlined methods. It was possible to reconstruct a published disease model. **CONCLUSIONS:** Ongoing research is conducted with focus on data quality, i.e., accuracy, completeness and timeliness, at the regional cancer registry.

PRM148

CONTINUOUS PATIENT ENGAGEMENT IN COMPARATIVE EFFECTIVENESS RESEARCH (CER): AN APPLICATION IN CARDIOVASCULAR DISEASE (CVD)

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OBJECTIVES: A 10-step, systematic framework to enhance patient engagement throughout the CER process has been previously proposed. The objective of this research was to apply this framework in the context of CVD since CVD is the leading cause of death in the United States and impacts a diverse patient population. **METHODS:** At each of the 10 steps in the research process, the rationale and means for researchers to engage CVD patients is presented. **RESULTS:** When prioritizing CER topics, patients can inform whether resources should be allocated towards hypertension, a highly prevalent disease with various established therapeutic options, or into finding new treatment options for patients affected by pulmonary arterial hypertension, a rare disease. Patients with CVD can also help to select outcomes that are meaningful from their perspective. Interest in the major outcomes (stroke, heart failure) will likely be balanced against patient concerns with treatment side effects, such as dizziness and dry cough, which can impact quality of life. In the latter steps of translation and dissemination, patients can help to tailor results under primary, secondary, or tertiary prevention and across racial/ethnic subgroups. **CONCLUSIONS:** The 10-step framework can be tailored to engage patients with CVD. For some stages of CER, purposes and strategies for patient engagement for CVD are similar to many other disease states. However, there are unique best practices for patient engagement in CVD. Researchers should recognize that there is no "one-size-fits-all" approach to patient engagement and should engage CVD patients throughout the CER continuum.

PRM150

VALUE OF RARE DISEASE NON-INTERVENTIONAL STUDIES TO SUPPORT PAYER & CLINICAL DESCISION MAKING

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OBJECTIVES: In rare diseases and sub-populations for specialty diseases, national and regional payer negotiations regarding funding and reimbursement of new drugs can be challenging due to the lack of available robust data to inform decision making. Clinical trials designed to ensure regulatory approval often lack the necessary information to meet the needs of a diverse range of payer and clinical stakeholders across the globe. Traditional patient registries, if available, generally do not capture the required level of detail, especially in terms of health-economic data. To ensure ongoing access, new therapies to treat rare diseases require further real world evidence to build a strong clinical and economic case for long term treatment provision. **METHOD:** We employed a variety of traditional and innovative methods to collect real-world evidence on disparate populations of patients with rare diseases. Retrospective chart review studies have been conducted to understand demographics, clinical and pathological characteristics, treatment, outcomes and resource use. Patient and caregiver surveys have subsequently been used to correlate quality of life, functional status and economic burden to patient treatment pathways. **RESULTS:** Non-interventional studies provided a longitudinal understanding of patient care pathway from diagnosis to long-term treatment and follow-up including the natural history of a rare disease, genotypic/phenotypic variability, differences in treatment patterns across countries and the clinical drivers of therapy use. This enabled comparison of real-world treatment practice versus clinical guidelines. In addition, direct and indirect costs were calculated to understand the budget impact of treatment. Insights helped the manufacturer refine the product value proposition and provide necessary evidence to support product access and reimbursement. **CONCLUSIONS:** Rare disease non-interventional studies offer manufacturers the opportunity to fulfill peri and post-launch evidence needs of regulators and payers by providing bespoke and robust real world data efficiently.

PRM151

PUBLICATION OF METHODOLOGICAL GUIDELINES: THE DEVELOPMENT OF SYSTEMATIC REVIEWS (SR) AND META-ANALYSES OF RANDOMIZED CLINICAL TRIALS BY THE DEPARTMENT OF SCIENCE AND TECHNOLOGY OF THE BRAZILIAN MINISTRY OF HEALTH (DECIT/MOH)

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Since 2004, DECIT supports the production of SR by teaching and research institutions in Brazil. However, these studies were guided by international recommendations causing some variability in the execution and presentation of results. In order to standardize and equalize the elaboration quality of SRs throughout Brazil, DECIT requested to research institute Hospital do Coração Hcor draft this guideline. The initiative was funded by the Support Program for the Institutional Development of the Brazilian Public Health System. The guideline was based on two international

guidelines used in clinical research: The Cochrane Reviewer's Handbook and a guideline prepared by the The Australian National Health and Medical Research Council. The aim of the guideline was to introduce the main concepts through a language that is more simple and accessible to health care professionals, familiar or not with the methodology of systematic reviews and meta-analyses. This guideline covers the three phases of a SR: planning, production and reporting of the SR. It does not take into account the impact of the type of question in the review process and does not exhaust all the mechanisms necessary in order to understand and perform a meta-analysis. It also presents the detailing of some fundamental concepts needed to conduct the systematic review in the form of appendices. In 2011, it was given the first version of the guideline. DECIT was responsible for the review and publishing of the final document. In 2012, the first issue of the guideline was published. The importance of the guideline is to orient and standardize the preparation and production of a quality SR, mainly due to the gap that exists in the national literature.

PRM152

COLLECTING PROS IN PATIENT REGISTRIES: THE NEED FOR AND POTENTIAL IMPACT OF PROVIDING PRO DATA TO THE TREATING PHYSICIAN – AND WHEN

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The advent of ePROs and direct-to-patient reporting has enabled patients participating in registries to report their symptom or treatment experiences between physician visits, with minimal patient burden. These independent reporting approaches are often used to support patient retention over long follow-up periods, and/or to collect patient-reported data outside of typical physician visit schedules. When a patient completes PROs independent of a physician's presence (i.e., not completed at the physician's office and not entered by the registry site), the treating physician may not be aware of the patient's responses and may need to either proactively ask for this information or wait to obtain this information at the end of the study. The move toward independent reporting of PRO data introduces several competing concerns. First, physician knowledge of the PRO responses could potentially alter the naturalistic follow-up in an observational study, if, for example, the physician's knowledge of the PRO response prompts him/her to alter the patient's treatment. As a result, patient reporting independence may be preferred from a research purity perspective. However, any PRO response that may be a safety signal would carry ethical considerations; in such a case, reporting independence would not be preferred. If patient care is always paramount to the benefits of research, then it could be argued that the optimization of patient care is only possible when the physician has all available patient information (e.g., PROs) at his/her disposal, in as close to real-time as possible. In addition, some research indicates that patients are more likely to complete PROs when their physician is aware of and using the PRO data to inform treatment decisions. Further discussion will focus on sponsor and researcher responsibilities for funneling observed data on a patient's experience back to the treating physician, drawing on examples from the literature and registry protocols.

PRM153

PRACTICAL APPROACHES TO ACHIEVING REAL-WORLD STUDY DATA REPRESENTATIVE OF THE TARGET POPULATION

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PURPOSE: To describe the most effective approaches to achieving a real-world study data sample that is representative of the target population. **DESCRIPTION:** Considerable attention is paid to the design and analysis of outcomes research studies to address internal validity by minimizing bias and confounding. However, too often, study sample populations are simply assumed to be representative of the study populations from which they are drawn, or are assessed for their representativeness only after the study has been conducted. Ideally, sample estimates should be as close as possible to their population value in order to make inferences about that study population. Practical implementation of measures to avoid selection bias and ensure a robust sampling procedure can be problematic. Challenges include, willingness of sites and patients to participate in research (convenience sampling), and management of site and patient drop-out after the study has begun. While many database studies and patient registries carry very large sample sizes and therefore begin to approximate the target population simply by means of sheer size, smaller studies may need to take steps, through stratified sampling and enrollment caps, to ensure that the study sample is reflective of the target population. These stratification variables may be at the site level (e.g., physician specialty, geography), the patient level (age, gender, ethnicity, disease duration) or both. Temporal issues may also be problematic where studies performed in the past may not reflect rapid changes impacting today's target population. Following a brief overview of the design and analysis considerations, this presentation will focus on case examples, drawn from different organizations, of approaches to achieving a representative sample, highlighting some of the challenges intrinsic to real-world research. Best practice recommendations will be provided to guide researchers on the most effective approaches, including the use of reference populations within specific countries.

PRM154

UTILIZATION OF UNMANNED AIRCRAFT SYSTEMS (UAS) FOR EMERGENCY MEDICAL SITUATIONS IN RURAL COMMUNITIES: A VISION FOR THE FUTURE

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OBJECTIVE: We propose a paradigm and ranking system for potential medical applications of unmanned aircraft systems (collectively UAS). Over the past three decades, UAS have become a vital component to our armed forces, used notably for combat but also commonly used for work in intelligence, reconnaissance and surveillance data collection. Such are defined as an aircraft without a human pilot on board, operated either autonomously by computer or under remote control by a human pilot. **METHODS:** We performed a targeted literature search for medical applications of UAS and rank-ordered strengths and weaknesses according to emerging applications and corresponding difficulty, feasibility and cost. **RESULTS:** Based on secondary sources, we report conceptual factors that can contribute to the practicality and efficiency of UAS in emergency medical situations. These were 1) frequency of occurrence, 2) time-sensitivity of occurrence, 3) rurality and complex terrain, 4) financial impact and 5) cultural acceptance. The results of our matrix point to a gradation of accepted uses for UAS with the variance in geographical location and urgency directly relating to an increase in operation costs. It is well known that natural disasters are increasing in frequency and intensity. Salient platforms for using UAS in medical delivery would be in the areas of natural and combative disaster relief. During these occurrences the use of UAS to aid in the medical relief could be a great asset. **CONCLUSION:** Our model illustrates how Big Data can be leveraged to improve ongoing quality and efficiency of UAS-delivered medical supplies, reduce time for delivery of supplies during times of natural disasters, and thus eschew our reliance on manned aircraft to assist in critical and non-critical medical operations.

PRM156

PUBLICATION MANUAL OF BUDGET IMPACT ANALYSIS (BIA) BY THE DEPARTMENT OF SCIENCE AND TECHNOLOGY OF THE MINISTRY OF HEALTH (DECIT)

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The epidemiological and economic methods applied to health technologies evaluations had a significant development in the last two decades. The need to balance the incorporation of new technologies in health care and limited financial resources promoted the construction and application of instruments supporting the decision making of health technology. The requirement Budget Impact Analysis formally stated in Law 12.401/2011 establishing the incorporation process technologies in SUS. In this context, in 2010/2011, the National Agency of Sanitary Surveillance (ANVISA) and DECIT, in partnership Institute for Health Technology Assessment (IATS) for drawing up of this guideline. In the first stage of development were used international recommendations of Canada, Australia, the UK and Poland, the recommendations of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the methods used in studies of budgetary impact that had already been published. Afterwards, drafted a preliminary version of the Guideline and a standard tool - Excel worksheets - to estimate the uptake of monetary resources required for adoption of new technologies. Revisions were carried out by technicians DECIT and health agencies, and the proposal was submitted to the Working Group on Development of Methodology REBRATS, composed of experts and academic researchers from several Brazilian states. Were also carried out workshops for the application of spreadsheets. In 2012, the first edition of the Guidelines was published two thousand copies in Portuguese in order to provide best practice recommendations for studies of budget impact.

PRM157

MIXED METHODS FOR THE DEVELOPMENT OF CLINCIAL OUTCOME ASSESSMENTS (COAS): EXPLORING FURTHER POSSIBILITIES FOR MIXED DATA COLLECTION AND ANALYSIS

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Mixed methods are fast becoming the go-to methodology for the development and validation of clinical outcome assessments (COAs). Although mixed methods have become popularized for COA development, most of this attention has focussed on Rasch measurement theory (RMT). However, the potential utility of mixed methods in COA development goes beyond RMT. There is a well-established literature base exploring the use of mixed data collection and crossover analyses in social research and many of these approaches can be readily applied to COA development. Thus a toolkit of methods is proposed which can be pragmatically selected to support the development of interpretable and purposeful COAs. Further integration of qualitative and quantitative data throughout the COA development process can serve to continually test the evolving hypothesis of the measurement construct and aid in evidence triangulation. Data can be transformed to create new data through 'quantitizing' qualitative data and 'qualitizing' quantitative data. Qualitative data collected during concept elicitation can be converted into binary code allowing development of inter- and intra-respondent matrices to explore the frequency and intensity of concepts. These data can be subjected to factor, correlational and regression analyses to explore the hierarchical structure and inter-relationships of qualitatively-derived themes and variables. Concept mapping techniques also allow the translation of qualitative data into pictorial form to show "clusters" of, or inter-relationships between, concepts. This collaborative approach involves stakeholders as partners in the research to generate, sort and rate items into conceptual models using statistical analyses. There are exciting opportunities to build upon existing practice and advance mixed research approaches in the field of COA development. Integrating mixed data collection and crossover analyses can enhance the interpretability and purposefulness of COAs ensuring they are developed with an evolving hypothesis and fit for purpose. The application of such methods for regulatory COA development requires further exploration.

PRM158

SIMULTANEOUS ITEM DEVELOPMENT (SID) FOR CLINICAL OUTCOMES ASSESSMENTS (COAS)

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